

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL SEARCH REPORT**

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 43179PCX364	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/NZ2004/000333	International filing date (day/month/year) 22 December 2004	(Earliest) Priority Date (day/month/year) 22 December 2003
Applicant AGRESEARCH LIMITED et al		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b.  With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2.  Certain claims were found unsearchable (See Box No. II).

3.  Unity of invention is lacking (See Box No. III).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No.

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

b.  none of the figures is to be published with the abstract.

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**Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)**

With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

**a. type of material**

a sequence listing  
 table(s) related to the sequence listing

**b. format of material**

in written format  
 in computer readable form

**c. time of filing/furnishing**

contained in the international application as filed  
 filed together with the international application in computer readable form  
 furnished subsequently to this Authority for the purposes of search

2.  In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

**3. Additional comments:**

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## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2.  Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See Supplemental Box.

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to:  
claims 1-13 partially and 15-40 partially (as they relate to SEQ ID No: 11, and SEQ ID No: 12).

## Remark on Protest

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

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## A. CLASSIFICATION OF SUBJECT MATTER

CL : C12N 9/02, C12N 15/52.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
SEE ELECTRONIC DATABASE BOXDocumentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
SEE ELECTRONIC DATABASE BOXElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
WPIDS, MEDLINE, CAPLUS, AGRICOLA, BIOSYS, BIOTECHABS (neotyphodium lolii, cytochrome P450, indole, diterpene, lolitrem); GENE BANK, DGENE (SEQ ID NO: 11, SEQ ID NO: 12).

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	Young, C et al(2005) XXIII Fungal Genetics Conference at Asilomar, March 15-20 2005, Pacific Grove, California, U.S.A., Biochemistry and Secondary Metabolism Poster#548: "A platform of three gene clusters is required for the biosynthesis of the bioprotective lolitrem alkaloids."	
A	Young, C. et al (2003) Molecular Breeding of Forage and Turf, Third International Symposium, May 18-22 2003, Dallas, Texas, USA, Poster#64: "Molecular cloning and genetic analysis of a fungal endophyte symbiosis expressed gene cluster for lolitrem biosynthesis".	

 Further documents are listed in the continuation of Box C See patent family annex

## \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search  
5 April 2005Date of mailing of the international search report  
15 APR 2005Name and mailing address of the ISA/AU  
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**Supplemental Box**

(To be used when the space in any of Boxes I to VIII is not sufficient)

**Continuation of Box III**

The international application does not comply with the requirements of unity of invention because it does not relate to one invention or to a group of inventions so linked as to form a single general inventive concept.

Note that Rule 13.2 states that where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only where there is a technical relationship among those inventions involving one or more of the same corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The ISA has identified 11 separate inventions:

- Invention 1: ltmG (SEQ ID NOs: 1, 2, 17 and 18).
- Invention 2: ltmM (SEQ ID NOs: 3, 4, 19, and 20).
- Invention 3: ltmK (SEQ ID NOs: 5, 6, 21, and 22).
- Invention 4: ltmC (SEQ ID NOs: 7 and 8).
- Invention 5: ltmP (SEQ ID NOs: 9 and 10).
- Invention 6: ltmJ (SEQ ID NOs: 11 and 12).
- Invention 7: ltmQ (SEQ ID NOs: 13 and 14).
- Invention 8: ltmD (SEQ ID NOs: 15 and 16).
- Invention 9: cluster SEQ ID NO: 23.
- Invention 10 cluster SEQ ID NO: 24.
- Invention 11 cluster SEQ ID NO: 25.

The claims are directed to nucleotide/polypeptide sequences, obtained from *N. lolii* and *E. festucae*, defining enzymes proposed to be involved in lolitrem biosynthesis. Although all of the sequences share the feature that they are proposed to be involved with the lolitrem pathway, this does not represent a special technical feature.

Firstly, this feature cannot be a special technical feature because it is not novel. The lolitrem biosynthesis pathway (and members thereof) is known:

1. Young, C. et al (2003) Molecular Breeding of Forage and Turf, Third International Symposium, May 18-22 2003, Dallas, Texas, USA, Poster#64: "Molecular cloning and genetic analysis of a fungal endophyte symbiosis expressed gene cluster for lolitrem biosynthesis".

Secondly, this feature cannot be regarded as a special technical feature as there are no structural features or enzymatic properties that are representative of a single group of structurally or functionally related proteins/nucleic acids. In particular, none of the claimed sequences could be used to obtain the others, and the sequences do not represent a single class of genes nor do they share any significant homology.

Continued on Supplemental Box (2).

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**Supplemental Box (2)**

(To be used when the space in any of Boxes I to VIII is not sufficient)

**Continuation of Supplemental Box**

With respect to the clusters (SEQ ID NOS: 23, 24, and 25), these clusters simply represent a group of metabolically related genes in a structure that is well known and understood with respect to secondary metabolites in fungi (see Young, C. et al (2003)).

Where there is some homology between subgroup members, it is also appropriate to apply the Markush approach to subgroups of the claimed inventions. For example, members of the P450 subgroup claimed (ie SEQ ID NOS: 5, 6, 9, 10, 11, 12, 13, 14, 21, 22) share some homology. However, this homology is also present in other known members of the P450 family. As such, there is no common novel structure present in all of the sequences and there is no single recognised class or group of compounds embracing all the sequences claimed. Thus according to Markush, it is appropriate to classify the sequences in terms of the 11 individual groups and thus these groups represent 11 different inventions.